Issues Motivating the Collection of Occupational Exposure Data

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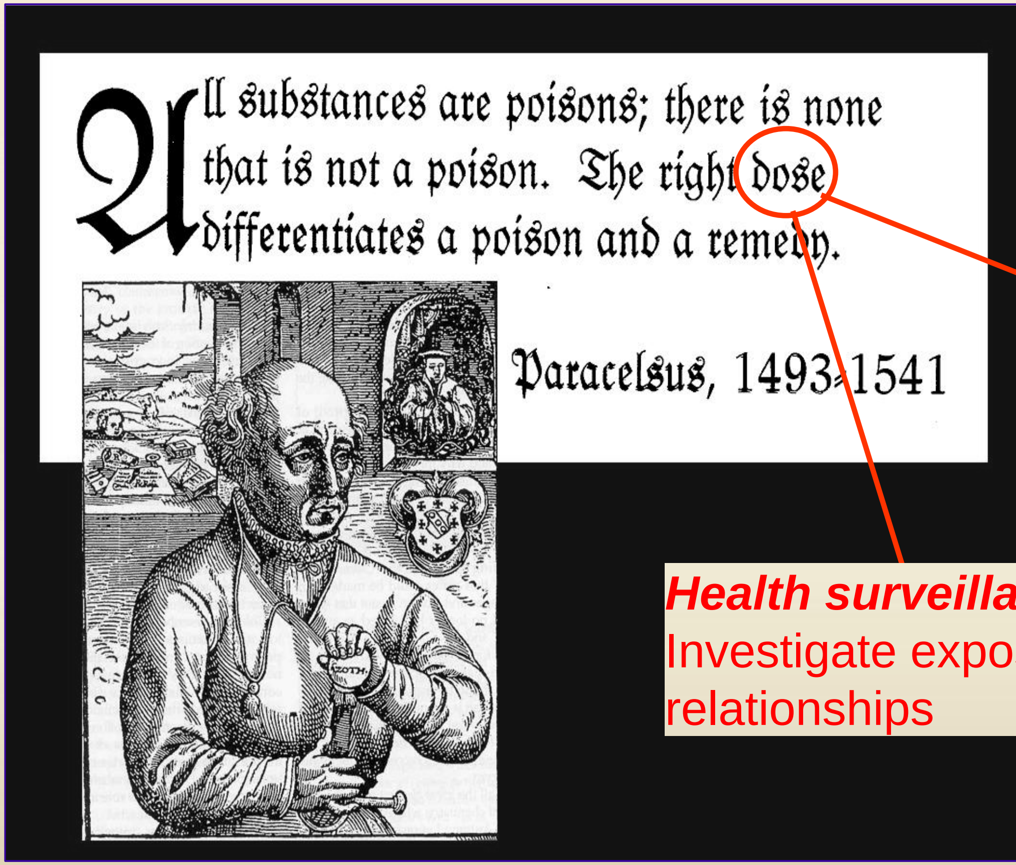
Topics

- Why measure airborne chemicals?
  - Hazard control v. health surveillance (epidemiology)
  - Air measurements v. exposures
- Evolution of air and exposure measurements
- Exposure variability and its sources
- How many measurements?
- If you build it will they come?
- Biomarkers of exposure

Why Measure Airborne Chemicals?



Hazard control: Setting and enforcing standards (OELs)

Health surveillance (epidemiology): Investigate exposure-(dose)-response relationships

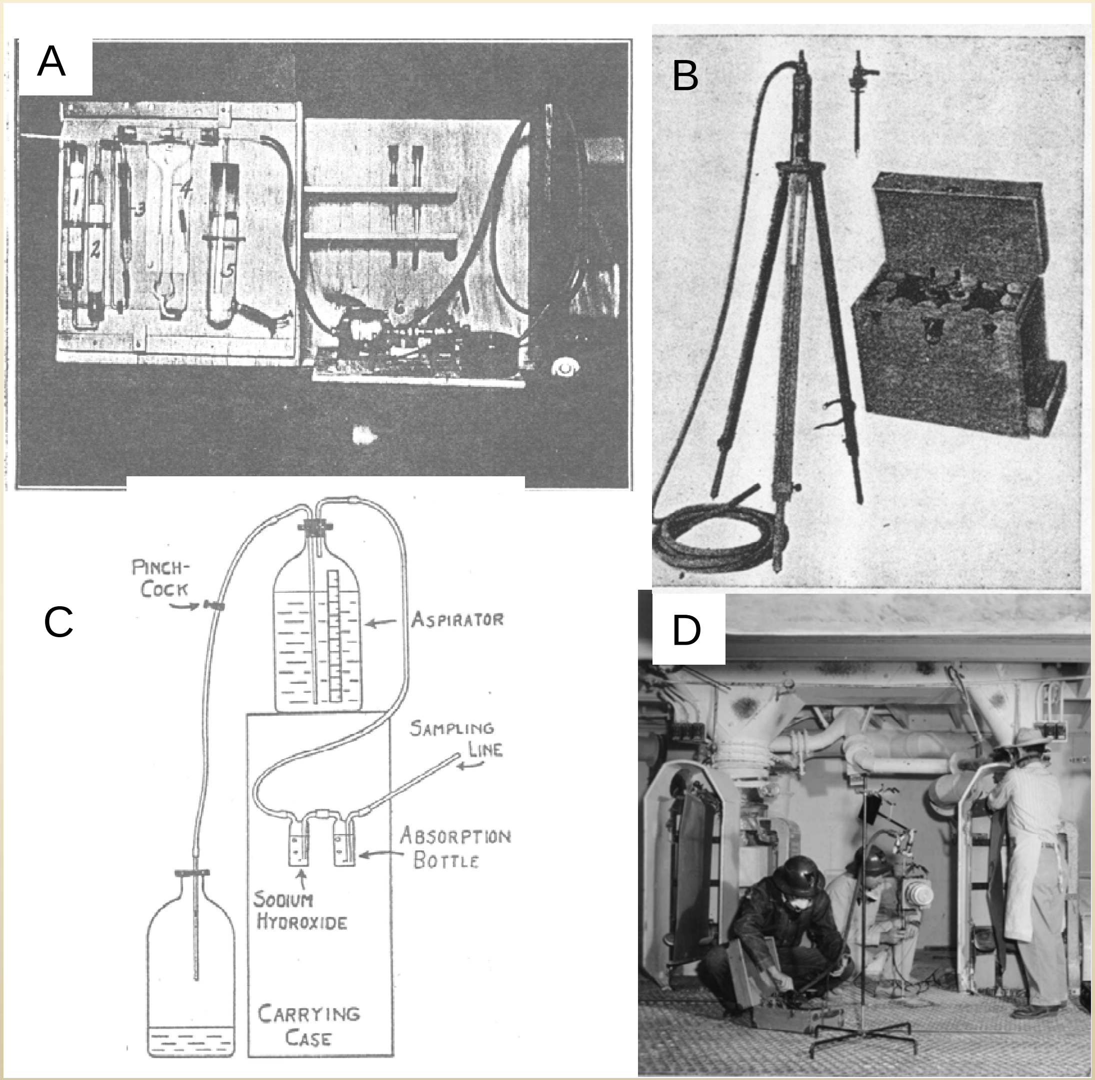
Health Surveillance v. Hazard Control

- Health surveillance (epidemiology)
  - Primarily focus upon long-term effects (years-decades)
    - Investigate exposure-response relationships
    - Best with extensive long-term quantitative *exposure* data
- Hazard control
  - Focus upon both short-term and long-term hazards
    - Short-term: (seconds–hours, e.g., H_2S, CO, NO_2, NH_3) Require *air (not exposure) measurements in some cases*
    - Long-term: (years-decades, e.g., benzene, PAHs, asbestos, heavy metals) Require extensive long-term *exposure* data

Evolution of Air and Exposure Measurements

Type	Air /Exposure	Time frame	Weight (g)	Assay
Area	Air	1920 - present	>1000	Lab
Breathing zone	Exposure	1940 - present	100 - 1000	Lab or direct
Personal	Exposure	1960 - present	10 - 1000	Lab or direct
Direct-reading (hand-held or personal)	Air or exposure	1980 - present	1 - 1000	Direct

Area Sampling: 1920s-Present
(Air measurements not exposures)



A: Collection of benzene by adsorption on charcoal about 1926 (Greenburg, 1926).
B: Greenburg-Smith impinger used for dust sampling about 1930 (Drinker and Hatch, 1936).
C: Collection of benzene by aspiration and absorption in acid about 1928 (Smyth and Smyth, 1928).
D: Collection of asbestos with a high-volume sampler and a cascade impactor about 1953 (Photograph courtesy of R. Herrick).

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Quantitative Exposure Assessment

Breathing-zone Sampling: 1940s – Present
(Moving from air measurements to exposures)

Two examples of breathing-zone sampling. Left: sampling with a midget impinger of explosive vapors (probably nitroglycerine) at an ordinance plant - USA (1943). US PHS . (Photograph courtesy of R. Herrick). Right: Benzene sampling with an explosimeter and silica gel tubes during manufacture of mechanical seals - UK (1950). (Photograph courtesy of R.J. Sherwood).

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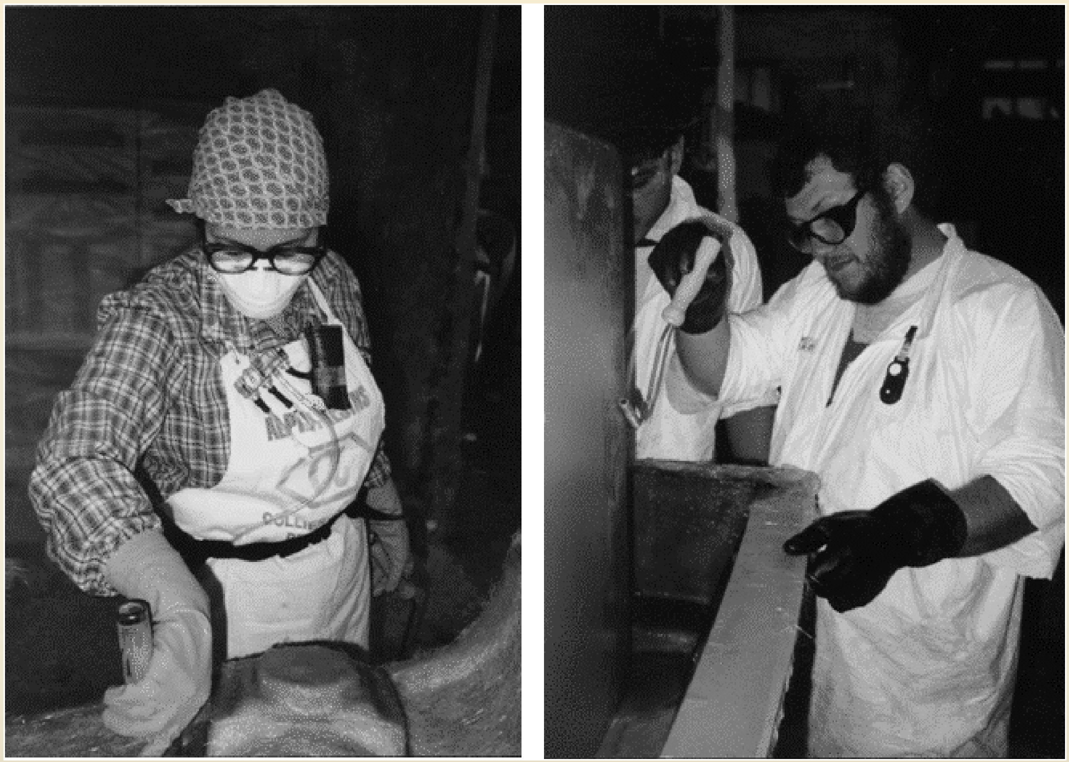
Personal Sampling: 1960s-Present (Exposure measurements)



Personal samplers to measure styrene, styrene oxide and MEKP in the reinforced-plastics industry- USA (1986). Left: active sampling with sorbent tubes and micro-impinger; Right: passive sampling with activated carbon (styrene and styrene oxide only).

Direct Measurements: 1980s – Present (Air measurements or exposures)

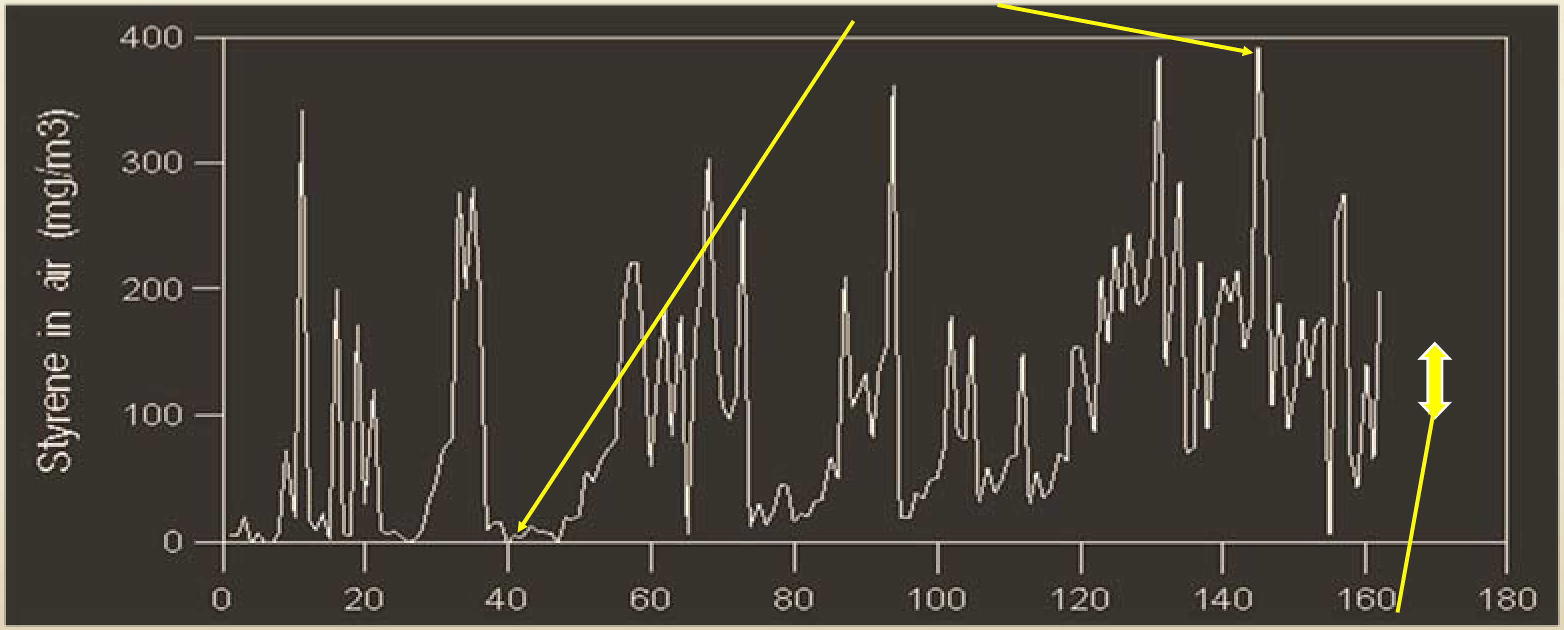
Hand-held devices (air measurements)

Direct-reading personal monitors (exposures)

Exposure Variability

Styrene levels in a boat factory (162 personal measurements - 1986-87)

1000-Fold Range



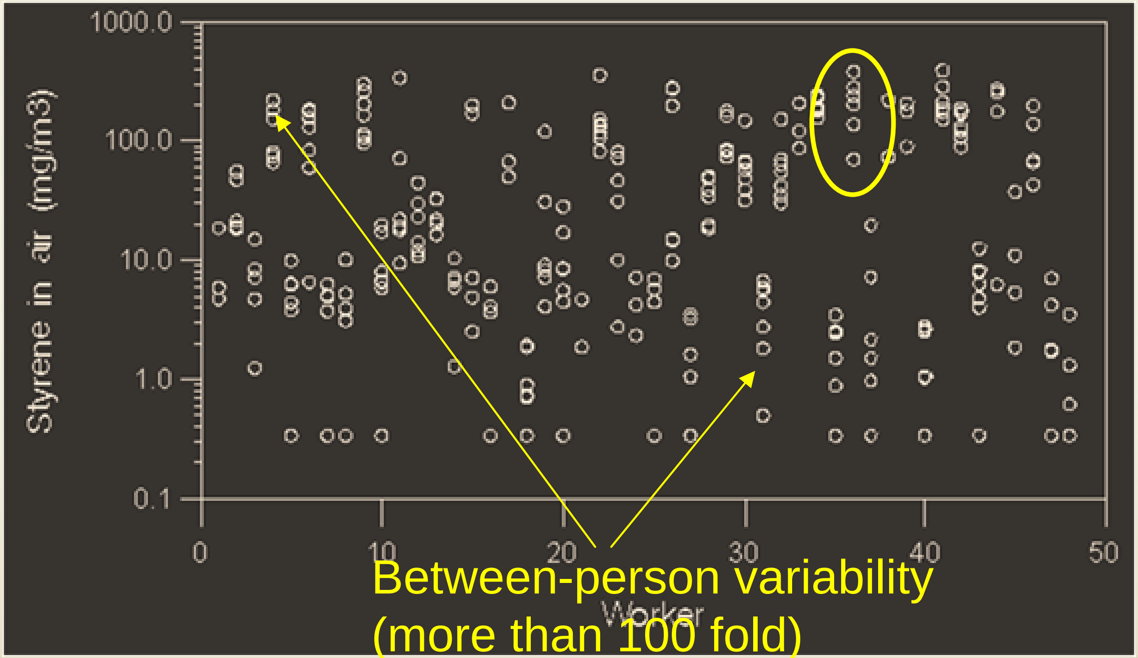
Air Sample

Assay error (0.2-fold)

Data from: Rappaport, *et al. Cancer Res*, 56: 5410-5416 (1996)

Within- and Between-Worker Variability

Within-person variability
(about 10-fold)

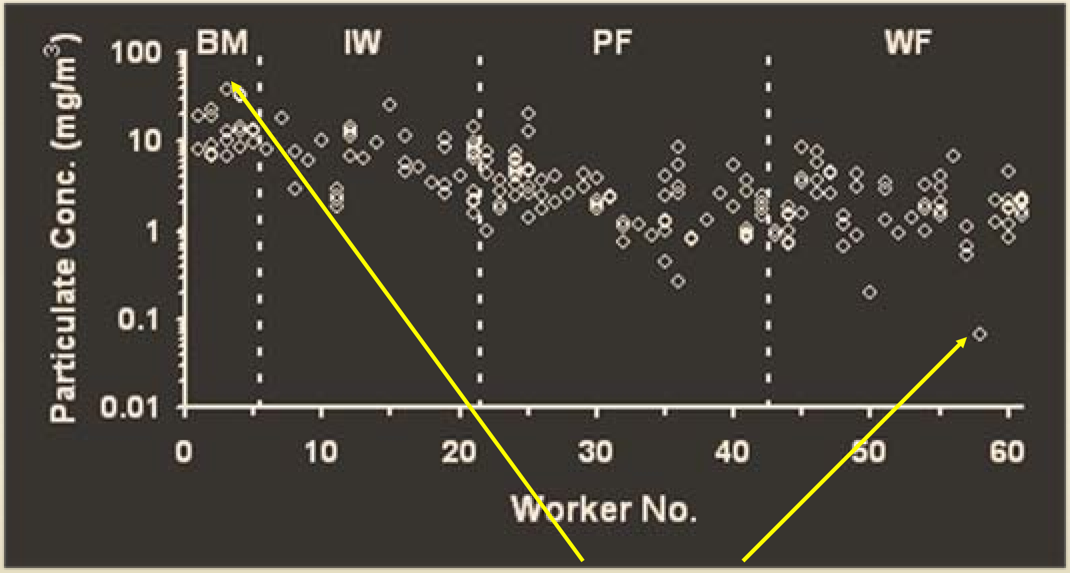


Data from: Rappaport *et al., Ann. Occup. Hyg.* 43:457-469, 1999

Exposure Variability

Welding-fume exposures among construction workers

(198 measurements from 62 workers in 4 trades – 1996-97)



1000-Fold range

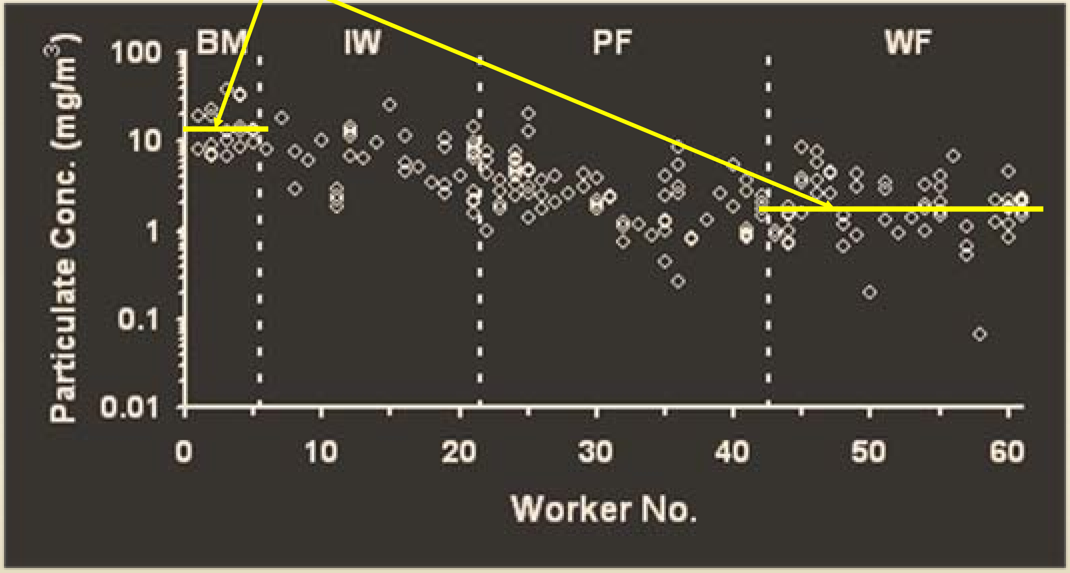
Data from: Rappaport *et al. Ann. Occup. Hyg.* 43:457-469, 1999

Exposure Variability

Welding-fume exposures among construction workers

(198 measurements from 62 workers in 4 jobs)

Group variability (4-fold)



Data from: Rappaport *et al. Ann. Occup. Hyg.* 43:457-469, 1999

Exposure Variability

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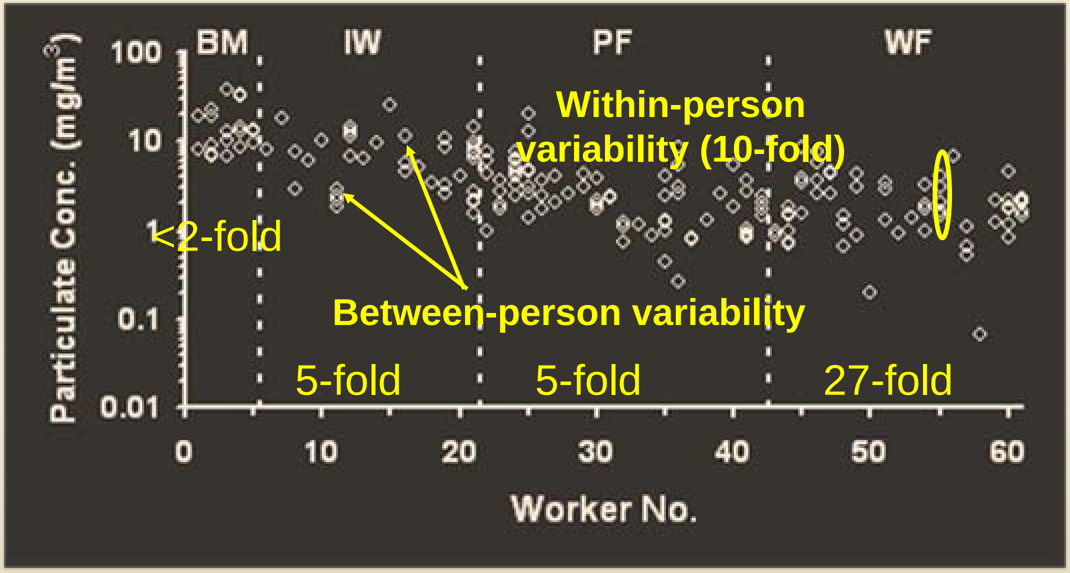

Data from: Rappaport *et al. Ann. Occup. Hyg.* 43:457-469, 1999

Determinants of Exposure to Welding Fumes (From fixed effect in mixed models)

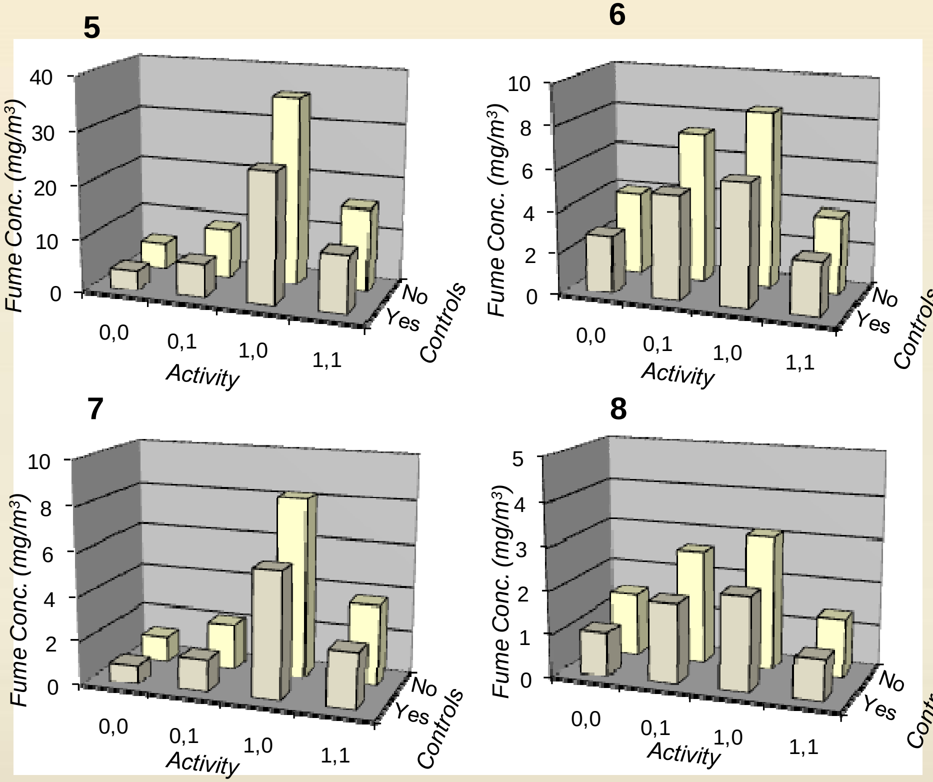

Fig. 7.6 Predicted mean exposures to welding fumes for Groups 5 - 8 (5=BM; 6=IW; 7=PF; 8=WF), based upon the model shown in Table 7.5. Activity (*IO*, *TW*): (0,0)=outdoor brazing/cutting; (0,1)=outdoor welding; (1,0)=indoor brazing/cutting; (1,1)=indoor welding. Controls consisted of local-exhaust or mechanical ventilation (*VE* = 1) and reduction of hot work to less than 50% (*CI* = 1). (Note that magnitudes of the y-axes differ across groups).

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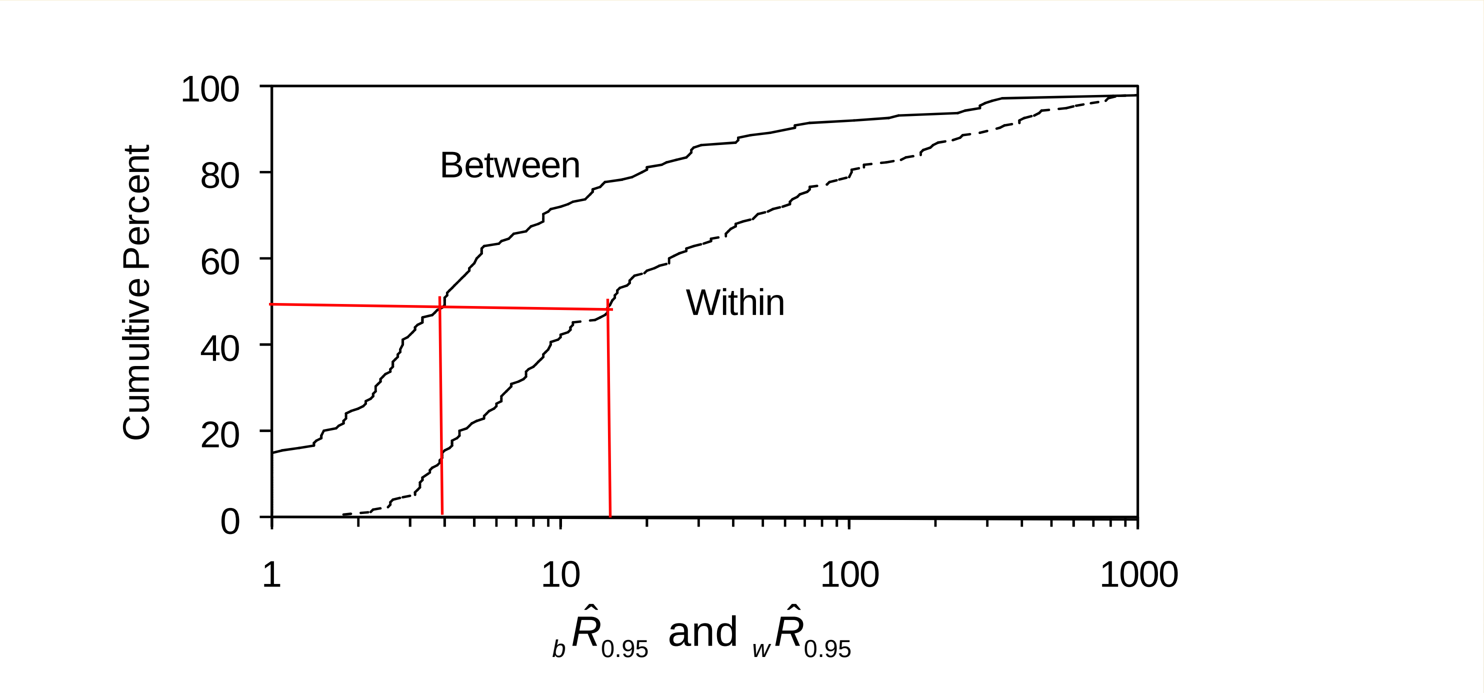
Variability Within and Between Workers



Between-worker = 4 fold: 95% of the workers in a given job group have mean exposure levels spanning a 4-fold range.

Within-worker = 15 fold: 95% of a typical worker's exposure levels vary 15-fold from day to day.

Rappaport and Kupper (2008) , *Quantitative Exposure Assessment, based upon work by Krommout et al. (1993)*

Variability Within and Between Workers: Not a New Idea!

Within-person and between-person sources of variability in exposure levels were recognized as early as 1952 when Oldham and Roach applied ANOVA models to breathing zone samples of dust in British coal mines (Oldham and Roach, 1952). They made the following observation:

> "It was found that significant variation was occurring in the dust concentrations from one collier's experience to another's, and from one day to another in the same collier's experience." (Note that a 'collier' is a coal miner).

Yet, this finding was largely ignored at the time, and the issue of within-person and between-person variability was not revisited again until some 35 years later when personal exposure measurements became available in occupational studies (Kromhout *et al.*, 1987; Rappaport *et al.*, 1988b; Spear *et al.*, 1987).

Rappaport and Kupper (2008)
Quantitative Exposure Assessment

Why so variable?

Multiplicative effects of several variables

- Jobs (fixed)
- Time (fixed)
- Locations (fixed or random)
- Sources of contamination (fixed or random)
- Activities and equipment (fixed or random)
- Worker/source mobility (mostly random)
- Environmental conditions (mostly random)

Implications of Exposure Variability

- Health surveillance (focus upon chronic health effects)
  - Many personal measurements needed to characterize *long-term exposures*
  - Longitudinal studies, evaluate variation within and between persons and across groups
    - Cannot assume all workers in a group are equally exposed
  - Advanced statistical models (mixed-effects models)
- Hazard control
  - Long-term hazards: same issues as above for health surveillance (repeated personal measurements, mixed modeling, etc.)
  - Short-term hazards: focus shifts to air levels/warnings of immediate dangers (*high air concentrations not exposures*)
    - Only most acutely toxic substances
    - Area sampling sufficient (e.g., confined spaces or at point of release)

Sample Sizes for Air Measurements (1920s – 1950s)

- Focus upon health effects (exposure-response)
- Few professionals (mostly governmental)
- Cumbersome equipment
- No OELs
- Few studies but relatively large sample sizes (hundreds of measurements)
  - Variability recognized
  - Desired accurate estimates of average levels for each location or factory
- Classic study of Oldham and Roach (1952)
  - 779 Breathing zone measurements (3-min) randomly collected repeatedly from Welsh coal miners

Repeated Random Measurements

APPENDIX

RESULTS OF "RANDOM COLLIERS" SURVEY

Collier	Total Time Spent on Coal-face (min.)	Duration of Mid-shift Break (min.)	Thermal Precipitator Samples (No. of particles per ml. between 0·5 and 5·0μ)											
1	315	25	1,630	800	1,100	920	1,500	1,770	980	1,430	1,540			
	430	15	950	<100*										
2	—	—	*Collier no longer working at pit*											
3	350	20	<100	1,320	650	<100	<100	360	(<100)†	<100	220	180		
	365	20	800	1,180	1,130	880	430	430	390	360	460	440		
4	345	20	1,750	1,690	2,030	2,730	1,980	940	1,360	2,070	2,190	830	2,650	
5	—	—	*Collier absent on both occasions*											
	—	—												
6	270	20	570	<100	<100	(210)	310	740	2,000	520				
	335	25	240	170	450	560	320	280	(<100)	320	520	820	520	510
7	325	40	390	700	920	1,240	1,580	1,530	920	530				
	365	35	1,110	730	(<100)	(<100)	750	1,090	720	1,130	580	770		
8	300	25	580	770	470	(<100)								
	395	25	350	1,460	800	1,250	1,150	1,010	(<100)	860	920	760	840	

A portion of an appendix originally published by Oldham and Roach (Oldham and Roach, 1952). Each entry represents the dust level for a random 3-min sample obtained from a coal worker. Note that several such measurements were obtained from each subject on a given day.

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First Application of Lognormal Distribution to Occupational Data

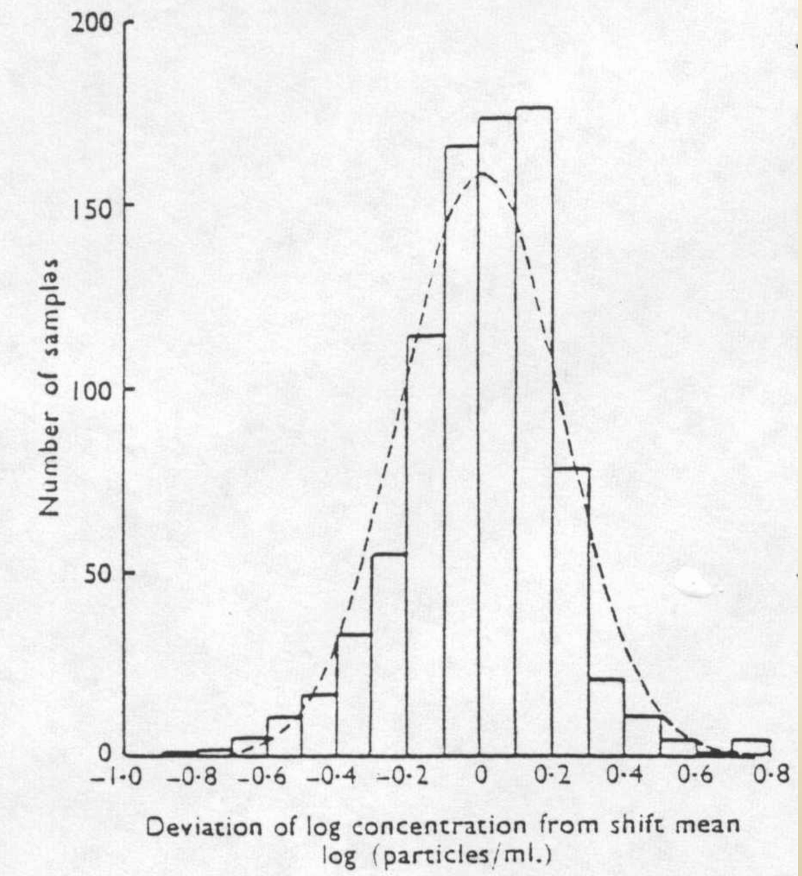

FIG. 2.—Distribution of deviations of 779 transformed samples from their shift means, with the Normal curve of equal area and standard deviation 0·2203.

Histogram of logged deviations of 779 breathing-zone measurements of dust in British coal mines [from Oldham (1953)].

Provides basis for advanced statistical modeling of data

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Exposure Data in Modern Epidemiological Studies

Only 13% of studies used quantitative measurements

Methods of exposure measurement 31

Table 2.2 Distribution of the main methods of exposure measurement (one selected from each study) in 564 studies of the aetiology of non-infectious disease published in the *American Journal of Epidemiology* between January 1980 and December 1989

Methods	Distribution (%)
Personal interview	49.1
Face to face	43.0
Telephone	4.1
Unclassifiable type	2.0
Self-administered questionnaire	14.0
By mail	6.4
Under supervision	7.6
Reference to records	22.3
Medical records	7.1
Other records	15.2
Physical or chemical measurements	13.3
On subject	10.8
On environment	2.5
Unclassifiable	1.2

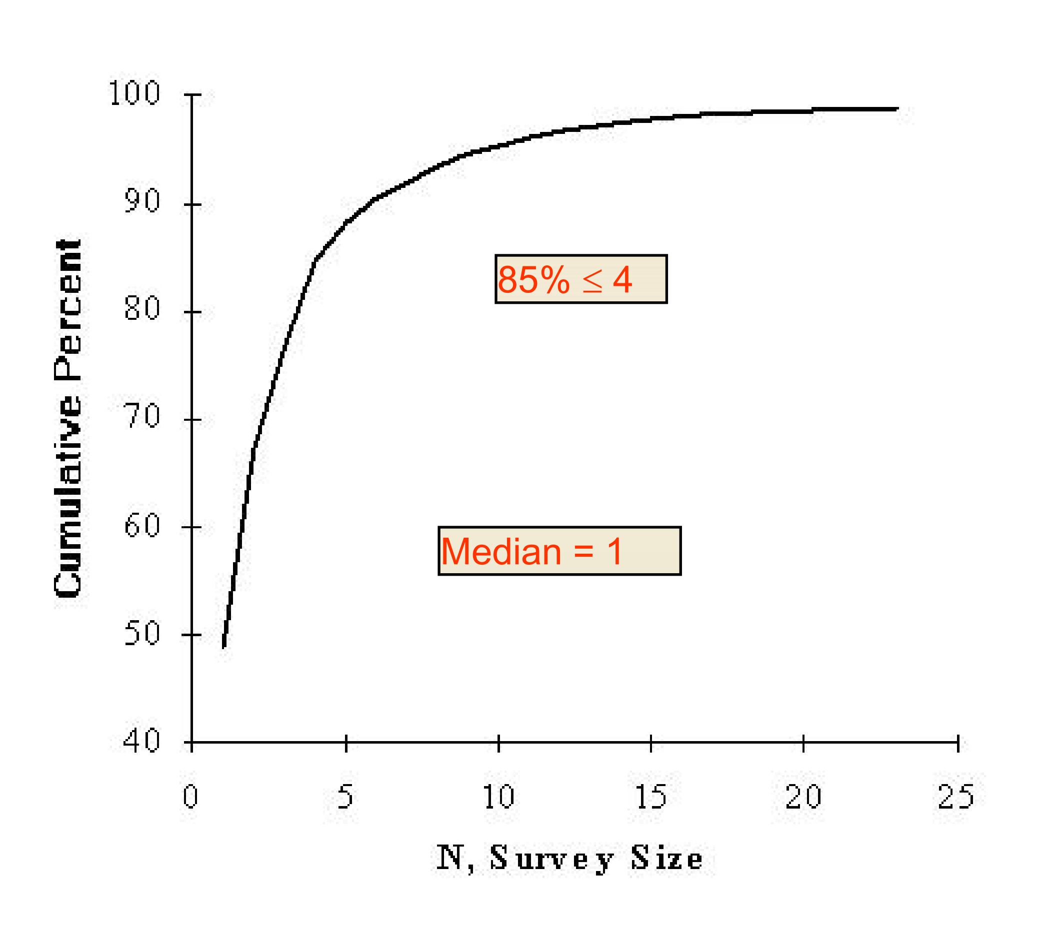
From: B.K. Armstrong *et al. Principles of Exposure Measurement in Epidemiology,* Oxford Med. Pubs., 1992

Sample Sizes for Workplace Measurements after OSH Act of 1970

- Many professionals (mostly employer-based)
- Advanced personal samplers and direct-reading monitors
- Focus upon hazard control rather than health surveillance
  - Only 16 new OSHA PELs since 1971
- Almost all air monitoring for acute hazards ('safety'), e.g., confined spaces, LEL, O_2 deficiency, substances IHTL
- Few measurements for chronic health effects
  - Median = 4 meas. from 696 published studies reviewed by Symanski *et al.* (1967-1996)

What about industrial surveys?

Sample Sizes for Industrial Surveys



Numbers of measurements obtained in 4864 annual surveys of occupational groups of workers in the nickel producing industry 1970 – 1990. [From (Tornero-Velez *et al.*, 1997)].

Better Equipment & More Professionals but Fewer Measurements – Why?

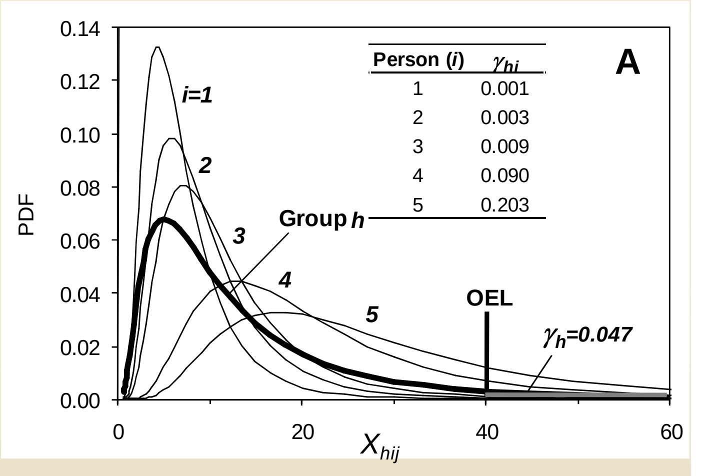
- Current trends
  - From government inspectors to employer-based inspectors (vested interests)
  - Increasing reliance on measurement–free methods (‘exposure models’, ‘control-banding’, etc.)
  - From exposure-response (long time frame) to *compliance* with OELs (short time frame)
- OELs have existed since the 1950s
  - Prior to 1970 OELs were guides
  - After OSH Act they became legal limits

Compliance Testing

- Rarely performed by OSHA inspectors
  - Fewer than 10,000 health inspections per year in 2.5 million US workplaces (P{health inspection} < 0.004/year)
- Vast majority performed by employers who must provide workplaces "…free from recognized hazards."
  - Company representatives (e.g., IH) *can* measure personal levels of persons in all groups with potential for excessive exposures
- One-to-one comparison of observed air levels with PEL
  - Compliance: All measurements < PEL
    - No additional measurements needed

Probability of Compliance

- Let γ_h represent the probability that a person in Group h would be exposed on one day above the OEL (exceedance of Group h)
  - $\gamma_h = \mathrm{P}\{X_{hij} > \mathrm{OEL}\}$



- Then the probability of compliance for Group h is

$$\mathrm{P}\{C_h\} = (1 - \gamma_h)^{N_h}$$

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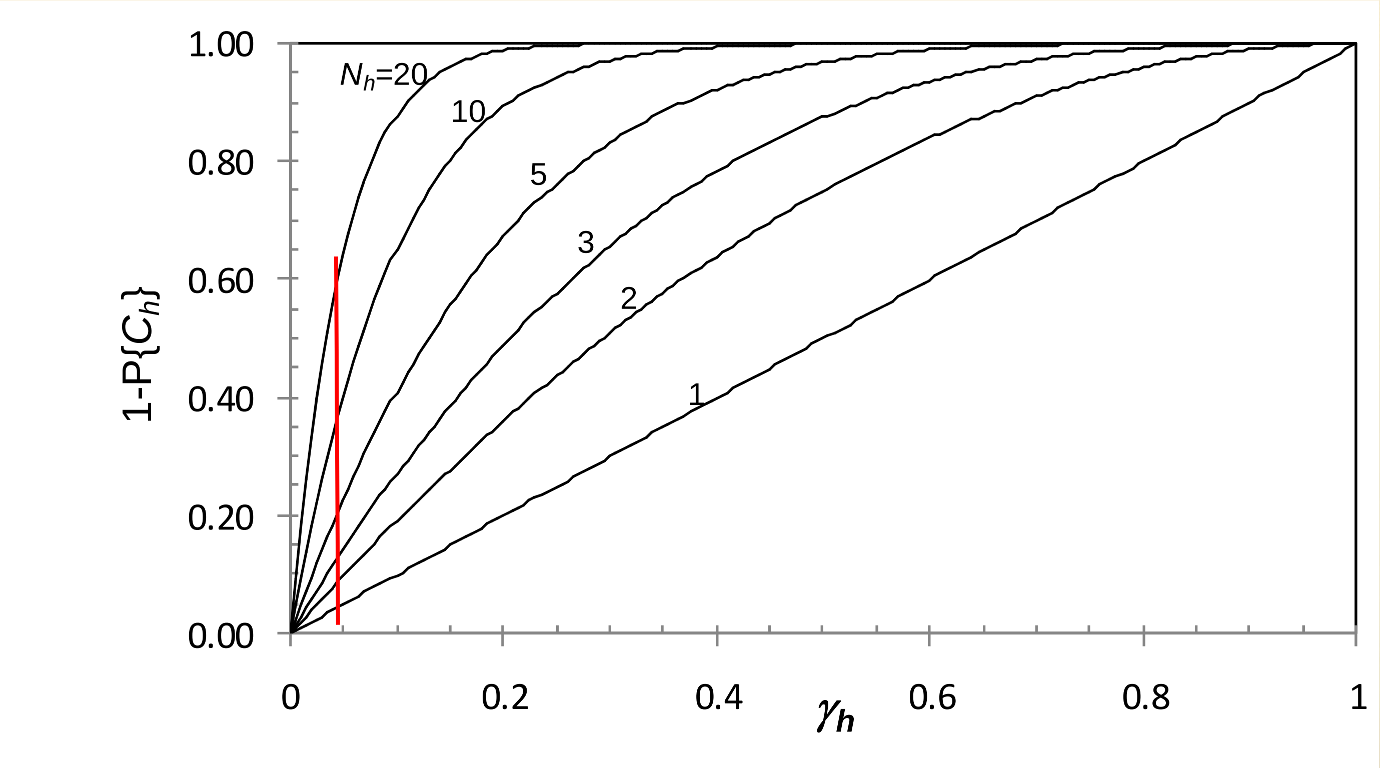
Noncompliance and Sample Size



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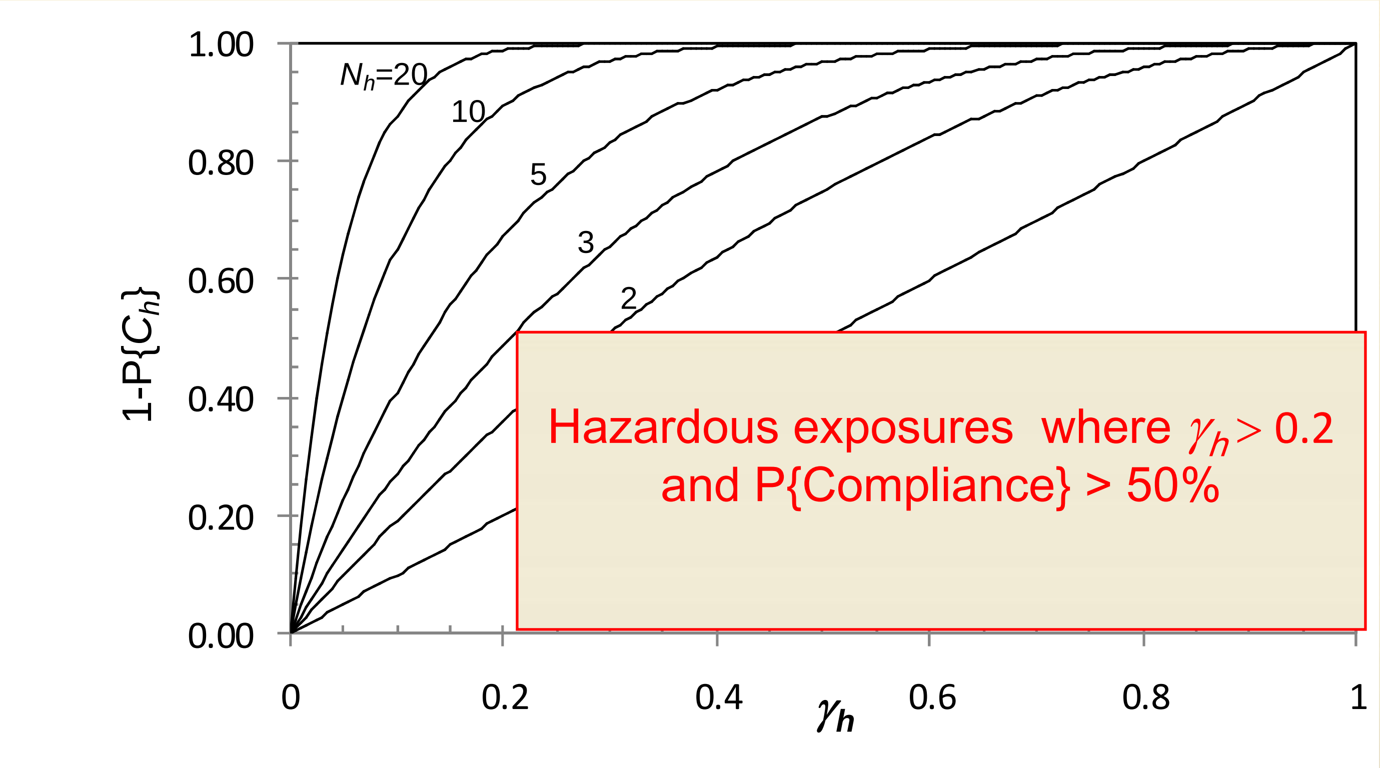

Since P{C_h} depends greatly on N_h, employers have incentive to maximize P{C_h} by making very few measurements *(Compliance testing can only be applied with small sample sizes)*

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Quantitative Exposure Assessment

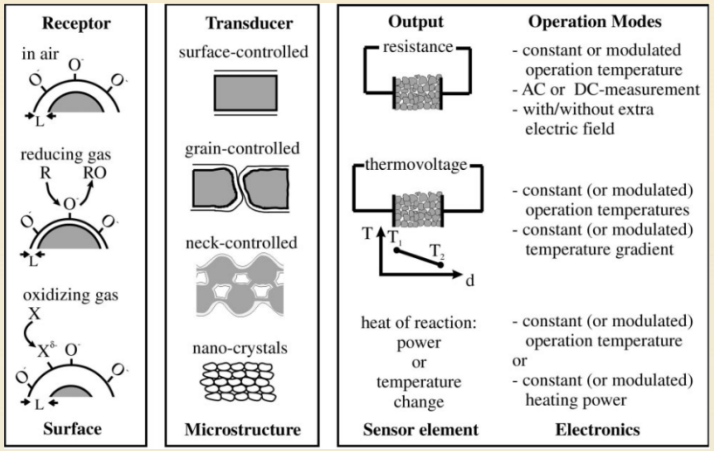
The Advantage of Air Monitoring

- OSHA standards mandate air monitoring for conditions IHTL (safety standards)
- Employers have incentives to avoid situations IHTL (confined spaces, trigger alarms, etc.)
  - Acute hazards easily assessed (reduces employer liability)
  - Hundreds of direct-reading air monitors commercially available
- Employers prefer to measure *air levels* of chronic toxicants because they are not clearly tied to *exposures*
  - Use of area rather than personal measurements
  - Evaluating air levels for tasks rather than workers
  - Can ignore between-worker differences in exposure

The Problem with Exposure Monitoring

- Under the OSH Act the burden of proof is upon the government to prove noncompliance with PELs
  - But there are essentially no government inspections (the OSH Act is based upon voluntary compliance!)
  - The use of compliance testing implicitly discourages *exposure* monitoring
- But - chronic health effects are slow to develop and difficult to relate to exposures without extensive exposure monitoring
  - Many employers don't want extensive exposure data in their files
- The situation is unlikely to change without a paradigm shift, such as REACH (**R**egistration, **E**valuation, **A**uthorization and Restriction of **C**hemical **H**azards) which places the burden of proof on the manufacturer to prove the safety of its products

If you build it will they come?
(You've got a DREAM …)



I. Simon et al. / Sensors and Actuators B 73 (2001) 1±26

Nanosensors of the future:

Ultra-small personal monitors

Multiple analytes

Data logging

Measure all workers' exposures – to everything - all the time!

Air monitoring

1920 1970 2008

Trends for measurements

None of the workers Ever

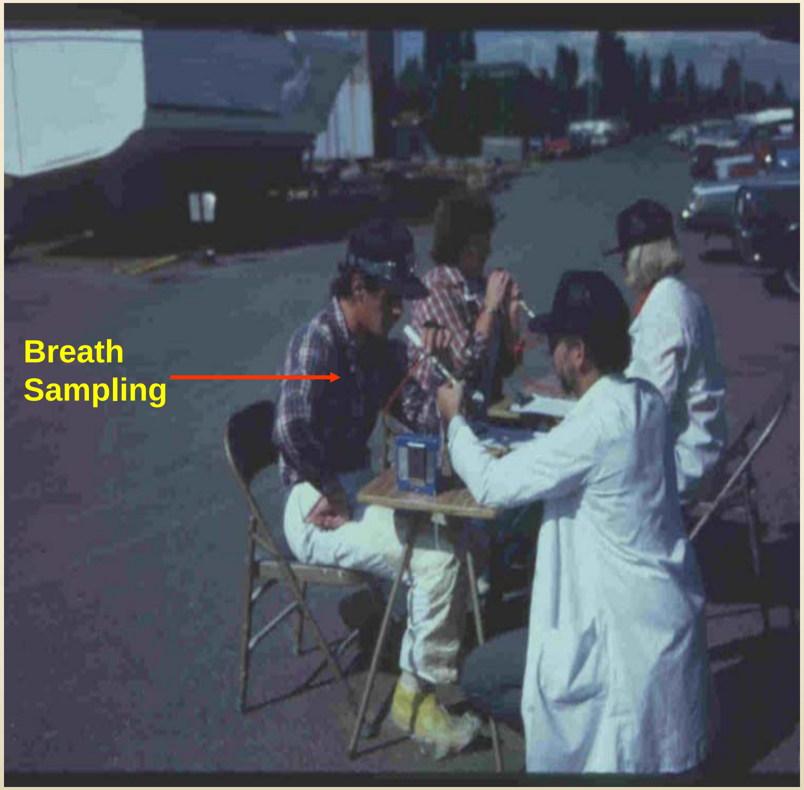
Half the workers Half the time

All the workers All the time

1920 2008

Exposure monitoring

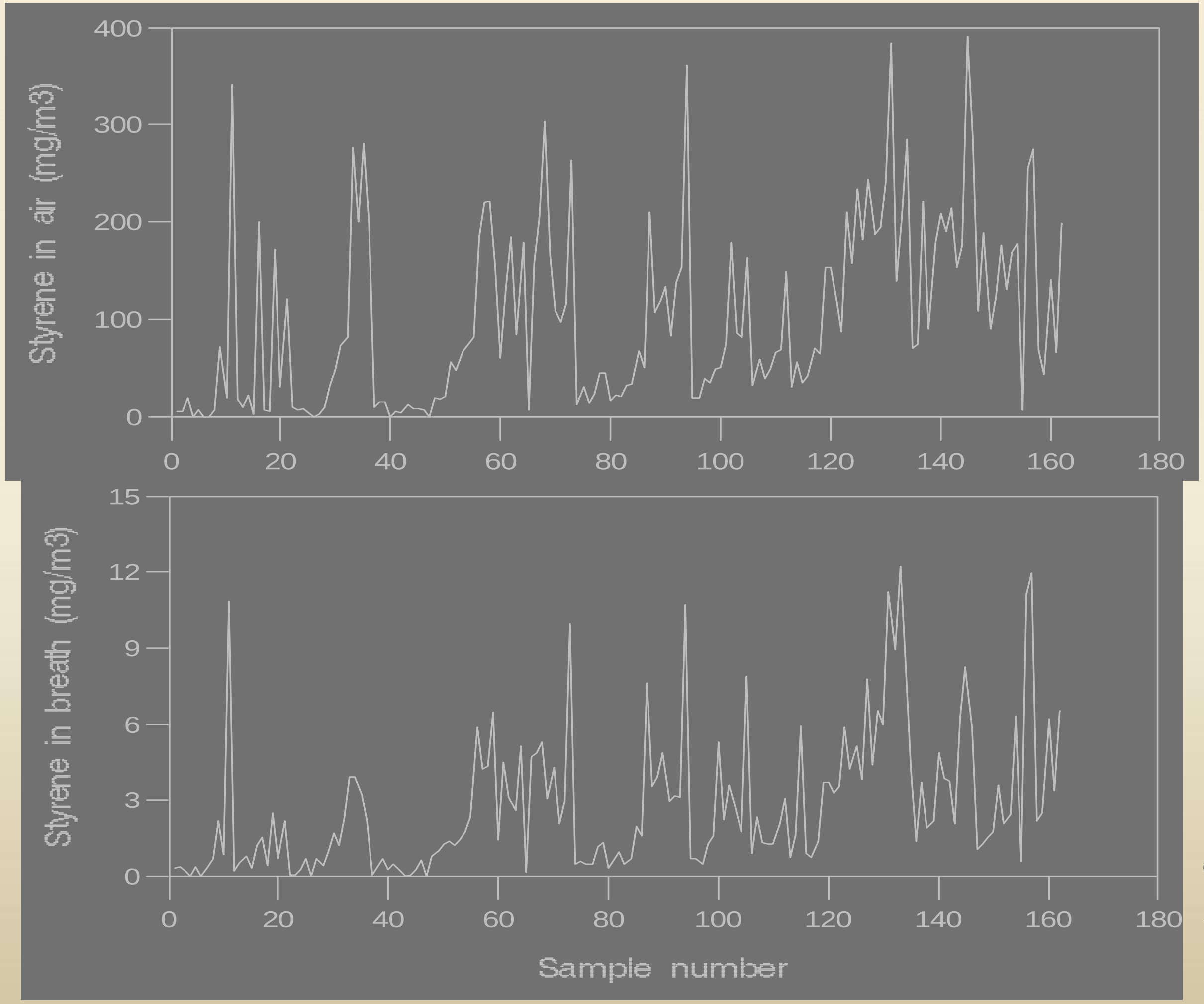
What about biomarkers of exposure?



Described in: Yager, et al. (1993) *Mut. Res.* 319:155-165.

Styrene in Air and Breath

Reinforced-plastics workers (3 – 7 meas./subj.)



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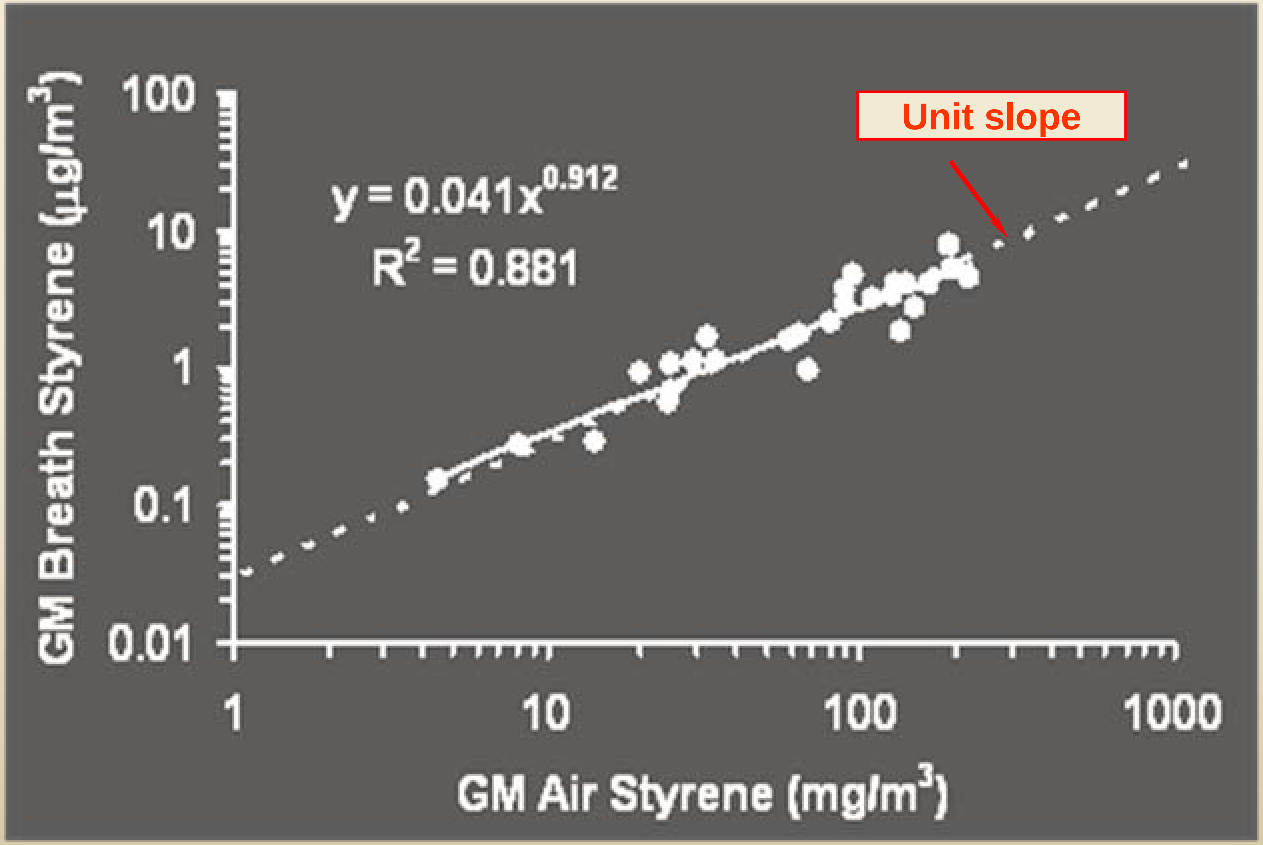

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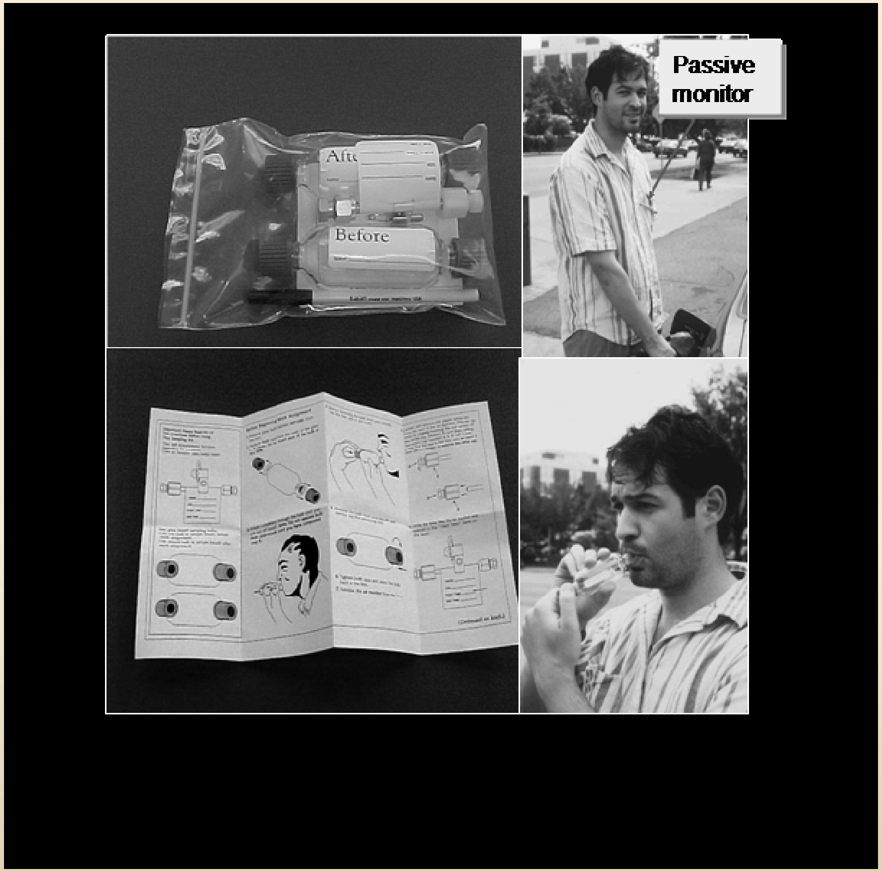
DREAM Biomarkers of Exposure

- Good idea
  - Highly relevant to exposure and health effects
  - When used with exposure measurements can illuminate important human kinetic processes
  - Adaptable to nanosensing and LOC systems (high throughput, multiple analytes)
- But U.S. employers don't like biomarkers (even less than personal exposure measurements)
  - Few OSHA standards require biomonitoring (Pb, Cd)
  - More demand in Europe, Asia, and for non-occupational exposures in the U.S.

Self-Assessment of Exposure



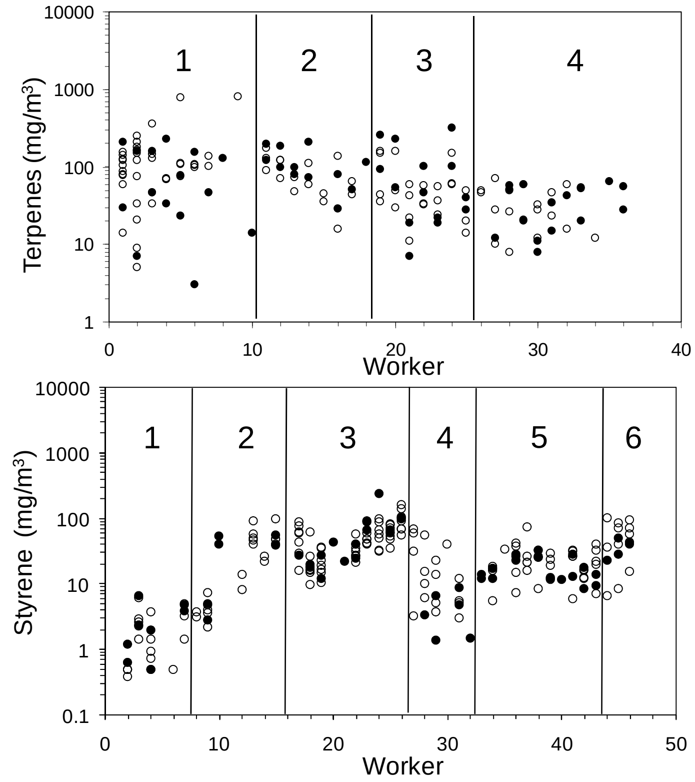


Fig. 3.2 Exposures to terpenes in sawmills (top) and to styrene in reinforced plastics factories (bottom). Open circles represent self-measurements made by workers and closed circles represent measurements made by an occupational hygienist on different days. Numbers represent different workplaces of a particular type. [Data from Liljelind *et al.* (2001)].

Rappaport and Kupper (2008)
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Take Home Messages

- Historically, exposure measurements were the holy grail that motivated breathing zone and personal sampling for studies of health effects
  - Early studies recognized exposure variability and included many measurements as a result

Take Home Messages

- Hazard control trumps health surveillance for contaminant measurements in U.S. workplaces
  - Regulatory focus is upon acute (safety) hazards not health hazards
  - Only 16 new OSHA standards in 37 years
  - Emphasis upon compliance with PELs discourages employers from monitoring exposures
  - Reinvigorating exposure monitoring will require a paradigm shift (e.g., REACH-type system)

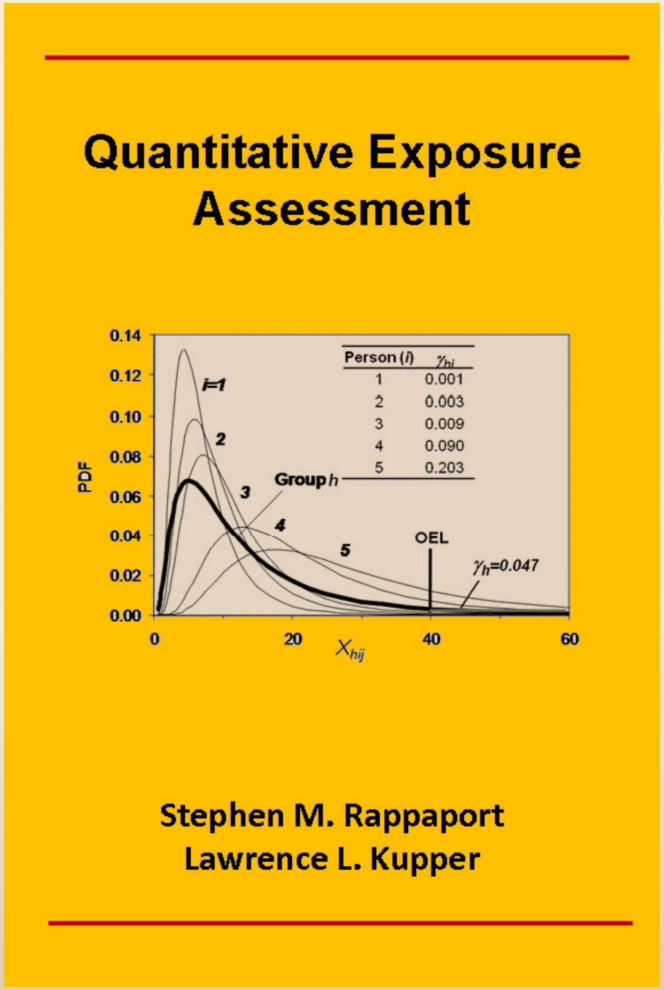
Take Home Messages

- Exposure levels vary tremendously across groups, between workers (within groups), and within workers over time
  - Puts a premium on repeated exposure measurements over the long term
  - Sophisticated statistical models needed to characterize exposures and their determinants

Take Home Messages

- Applications of DREAM technology for air (rather than personal) measurements are straightforward
  - Satisfy needs for control of acute hazards
- Extending DREAM to collect large numbers of measurements of personal exposure or biomarkers will require a shift in regulatory focus and/or enforcement

30 Years of thinking - in 183 pages



- The vagaries of exposure limits
- Measurement-based exposure assessment
- Statistical tools for exploring exposure variability
  - Within- and between-worker sources of variability
  - Determinants of exposure
- Implications for hazard control and epidemiology
- Choosing between environmental measurements and biomarkers

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